

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

We claim:

**Claim 1. (Currently Amended)** A method of screening for a substance which is useful in the treatment of a lipid metabolism dysfunction associated with apolipoprotein C-III, comprising

contacting said substance with a human Rev-erb receptor protein (hRev-erb) or a protein which at least comprises the hRev-erb ligand binding site and the hRev-erb DNA binding site;

providing a hRev-erb response element or a polynucleotide sequence onto which said Rev-erb receptor is capable of binding thereto; and

detecting the transcriptional activity of a gene which is under the control of a promoter comprising said response element in the presence and absence of said test substance,

wherein modulation of said transcriptional activity of said gene in the presence of said test substance indicates that said test substance is useful in the treatment of said lipid metabolism dysfunction associated with apolipoprotein C-III.

**Claim 2. (Previously Presented)** The method according to Claim 1, wherein the Rev-erb receptor is the hRev-erba receptor and the Rev-erb receptor response element is the hRev-erba receptor response element.

**Claim 3. (Currently Amended)** A process for screening a substance which is useful in the treatment of a lipid metabolism dysfunction associated with apolipoprotein C-III, comprising

placing a test substance in contact with a receptor of the human Rev-erb family (hRev-erb) or a protein which at least comprises the hRev-erb ligand binding site and the hRev-erb DNA binding site,

providing a human Rev-erb receptor response element or a polynucleotide sequence onto which said hRev-erb is capable of binding thereto,

providing a nuclear factor which is capable of functionally coupling the Rev-erb to an RNA-polymerase complex, and

measuring:

(a) (i) the binding of said test substance to the Rev-erb receptor or

(ii) the binding of a test substance-hRev-erb receptor complex to said hRev-erb response element and/or to a nuclear factor capable of functionally coupling said hRev-erb to the

RNA polymerase complex,

and

- (b) optionally detecting the modulation of transcriptional activity of a gene which is under the control of a promoter comprising the hRev-erb response element.

**Claim 4. (Withdrawn)** A process for screening substances which are useful in the treatment of lipid metabolism dysfunctions, comprising determining the effect of the test substance on the modulation of the expression of the gene coding for the Rev-erb receptor.

**Claim 5. (Withdrawn)** A method for the preparation of a pharmaceutical composition for the treatment of lipid metabolism dysfunctions associated with apolipoprotein C-III in man or animals comprising selecting a substance identified by a screening process according to Claims 3.

**Claim 6. (Withdrawn)** A method for the preparation of a pharmaceutical composition for the treatment and/or prevention of lipid metabolism dysfunctions associated with apolipoprotein C-III in man or animals comprising identifying a substance which is capable of binding to the Rev-erb receptor or to the response element thereof.

**Claim 7. (Withdrawn)** A method for the preparation of a pharmaceutical composition for the treatment and/or prevention of lipid metabolism dysfunctions associated with apolipoprotein C-III in man or animals comprising identifying a substance which is capable of modulating the transcriptional activity of a gene placed under the control of a promoter comprising the Rev-erb receptor response element.

**Claim 8. (Withdrawn)** A method for the preparation of a composition, for the treatment and/or prevention of lipid metabolism dysfunctions associated with apolipoprotein C-III in man or animals comprising identifying a substance which is capable of modulating the expression of the gene coding for the Rev-erb receptor.

**Claim 9. (Currently Amended)** A method for the characterization or testing <sup>[[5]]</sup> of the mechanism of action of a substance having anti-atherosclerotic properties comprising  
placing said substance in contact with a receptor of the Rev-erb family (hRev-erb) or a protein which at least comprises the hRev-erb ligand binding site and the hRev-erb DNA binding

site,

providing a human Rev-erb receptor response element or a polynucleotide sequence onto which said hRev-erb receptor is capable of binding thereto,

providing a nuclear factor which is capable of functionally coupling said hRev-erb to an RNA-polymerase complex, and measuring:

- (a) (i) the binding of said substance to the Rev-erb receptor or
- (ii) the binding of a test substance-hRev-erb receptor complex to said hRev-erb response element and/or to a nuclear factor capable of functionally coupling said hRev-erb to the RNA polymerase complex,

~~and~~

- (b) optionally detecting the modulation of transcriptional activity of a gene which is under the control of a promoter comprising the hRev-erb response element,

and

- (c) determining the mechanism of action of said anti-atherosclerotic compound based on assays (a) and/or (b).

**Claim 10. (Previously Presented)** The method according to claim 3, wherein said gene is apolipoprotein C-III (apo C-III).

**Claim 11. (Currently Amended)** The method according to claim 10 wherein a reduction in the transcriptional activity of said apolipoprotein C-III (apo C-III) in presence of said test compound indicates that said test compound is useful in the treatment of ~~a~~ said lipid metabolism dysfunction associated with apolipoprotein C-III.

**Claim 12. (Previously Presented)** The method according to claim 9, wherein said gene is apolipoprotein C-III (apo C-III).

**Claim 13. (Previously Presented)** The method according to claim 12 wherein a reduction in the transcriptional activity of said apolipoprotein C-III (apo C-III) in presence of said compound indicates that said compound has anti-atherosclerotic property.

**Claim 14. (Previously Presented)** The method according to claim 1, wherein the hRev-erb receptor protein is a chimeric protein comprising said hRev-erb receptor protein.

**Claim 15. (Previously Presented)**

The method according to claim 14, wherein the Rev-erb receptor protein is a chimeric protein comprising Rev-erb ligand binding site and maltose-binding-protein or a chimeric protein comprising Rev-erb ligand binding site and glutathione-S-transferase.